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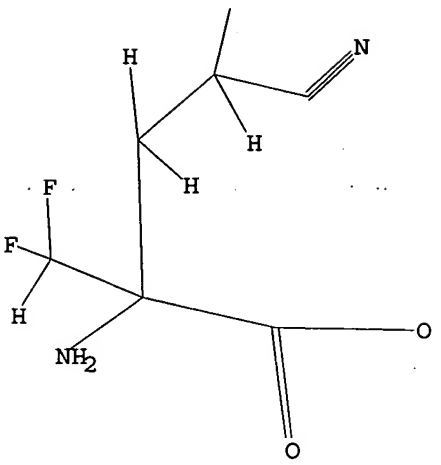
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 12:32:31 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 17 TO ITERATE

100.0% PROCESSED 17 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 93 TO 587
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

L3 0 L2

=> s l1 full
REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 12:32:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 314 TO ITERATE

100.0% PROCESSED 314 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L4 1 SEA SSS FUL L1

L5 1 L4

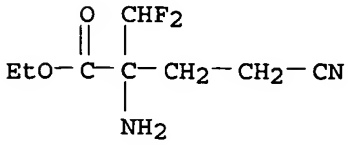
=> d ibib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:202415 CAPLUS
DOCUMENT NUMBER: 138:221839
TITLE: Processes for the production of α-difluoromethyl ornithine (DFMO)
INVENTOR(S): Zhu, Jingyang; Chadwick, Scott T.; Price, Benjamin A.; Zhao, Shannon X.; Costello, Carrie A.; Vemishetti, Purushotham
PATENT ASSIGNEE(S): Women First Healthcare, Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020209	A2	20030313	WO 2002-US26990	20020823
WO 2003020209	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003083384	A1	20030501	US 2002-224890	20020819
US 6730809	B2	20040504		
EP 1421058	A2	20040526	EP 2002-768695	20020823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ 531331	A	20040625	NZ 2002-531331	20020823
BR 2002012153	A	20040713	BR 2002-12153	20020823
JP 2005501881	T2	20050120	JP 2003-524523	20020823
US 2004171876	A1	20040902	US 2004-788728	20040226
PRIORITY APPLN. INFO.:			US 2001-315832P P	20010829
			US 2002-224890 A1	20020819
			WO 2002-US26990 W	20020823

OTHER SOURCE(S): CASREACT 138:221839; MARPAT 138:221839
AB Processes and synthetic intermediates for the preparation of H2NCH2CH2CH2C(CHF2)(NH2)CO2H (DFMO) are described. Thus, condensation of glycine Et ester hydrochloride with benzaldehyde (MgSO4/Et3N/MeCN), addition reaction with acrylonitrile (K2CO3/Et3N+CH2Ph Cl-), reaction with ClCHF2 (LiOBu-t/THF), and deprotection (4 N HCl/MTBE) yielded NCCH2CH2C(CHF2)(NH2)CO2H. Hydrogenolysis over 10% Pd/C in MTBE and treatment with 12 N HCl afforded DFMO.HCl (.apprx. 75 % pure by 1H NMR).
IT **501011-46-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(production of α-difluoromethyl ornithine)
RN 501011-46-7 CAPLUS
CN Butanoic acid, 2-amino-4-cyano-2-(difluoromethyl)-, ethyl ester (9CI) (CA INDEX NAME)



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                S L1

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     FILE 'CAPLUS' ENTERED AT 11:00:33 ON 10 FEB 2005
L3            3 S L2
L4            3 S 81645-68-3/PREP
L5            0 S 81645-68-3/PROC
L6            0 S 81645-68-3/PUR
                S L1

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L7           17 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 11:03:11 ON 10 FEB 2005
L8         1264 S L7 FULL
L9           12 S L8 AND (CYAN? OR NITRILE)
L10           1 S L9 AND REDUC?
L11           0 S L9 AND HYDROLY?
L12          16 S L8 AND HYDROLY?
L13           0 S L12 AND L9
L14           4 S L12 AND BASE
L15           0 S L9 AND L14
L16          28 S L9 OR L12 OR L14
L17          22 S L16 AND PY<2001

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L1 STRUCTURE UPLOADED

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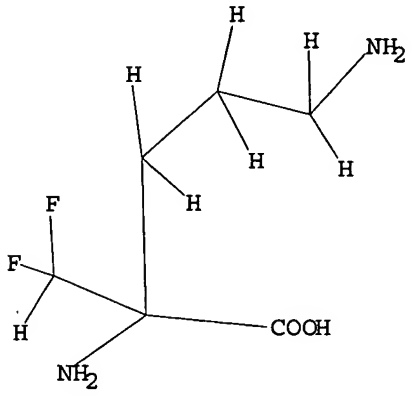
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 11:00:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 17 TO ITERATE

100.0% PROCESSED 17 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 93 TO 587
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

L3 3 L2

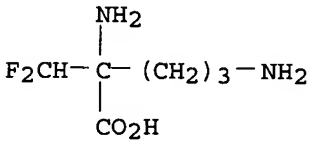
=> d 1-3 ibib abs hitstr

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:103892 CAPLUS
DOCUMENT NUMBER: 100:103892
TITLE: 2-(Difluoromethyl)-2,5-diaminopentanoic acid
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.

SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 53,937, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4413141	A	19831101	US 1982-419347	19820917
US 4438270	A	19840320	US 1982-392051	19820625
US 4496588	A	19850129	US 1983-487243	19830428
US 4560795	A	19851224	US 1984-577116	19840206
US 5614557	A	19970325	US 1995-403531	19950314
PRIORITY APPLN. INFO.:			US 1977-814765	A1 19770711
			US 1979-53937	A2 19790702
			US 1979-28757	B1 19790410
			US 1979-28758	A1 19790410
			US 1980-204749	B2 19801107
			US 1981-262834	B1 19810512
			US 1982-382265	B3 19820526
			US 1982-392051	A3 19820625
			US 1982-373198	A1 19820929
			US 1984-639977	B1 19840810
			US 1987-110639	B1 19871015
			US 1988-228789	B1 19880804
			US 1989-334733	B1 19890406
			US 1989-431685	B1 19891103
			US 1990-534008	B1 19900601
			US 1991-759633	B1 19910912
			US 1992-874989	B1 19920424
			US 1993-2521	B1 19930111
			US 1993-137397	B1 19931014
			US 1994-284706	B1 19940802

OTHER SOURCE(S): CASREACT 100:103892
AB The title compound (I) was prepared as an ornithine decarboxylase inhibitor (no data). Thus, solns. of (Me2CH)2NH and dibenzylideneornithine Me ester in THF were added to BuLi in hexane at -78° and ClCHF2 was bubbled in at 40-50° for 3 h to give I.HCl. The product could be resolved via its (-)-binaphthylphosphate salt.
IT **81645-68-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 81645-68-3 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:581486 CAPLUS
DOCUMENT NUMBER: 99:181486
TITLE: Inhibiting the growth of protozoa

INVENTOR(S): Sjoerdsma, Albert; McCann, Peter P.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 159,973, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

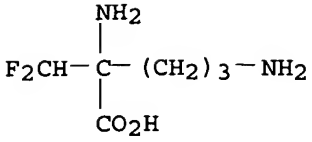
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4399151	A	19830816	US 1981-262275	19810511
SE 8103678	A	19811217	SE 1981-3678	19810611
SE 460517	B	19891023		
SE 460517	C	19900215		
AU 8171654	A1	19811224	AU 1981-71654	19810611
AU 544990	B2	19850627		
ZA 8103953	A	19820630	ZA 1981-3953	19810611
CA 1174603	A1	19840918	CA 1981-379588	19810611
DE 3123295	A1	19820429	DE 1981-3123295	19810612
DE 3123295	C2	19900712		
IL 63087	A1	19841031	IL 1981-63087	19810612
DE 3153623	C2	19910627	DE 1981-3153623	19810612
BE 889230	A1	19811215	BE 1981-205104	19810615
GB 2078735	A	19820113	GB 1981-18326	19810615
GB 2078735	B2	19850515		
NL 8102863	A	19820118	NL 1981-2863	19810615
NL 194153	B	20010402		
NL 194153	C	20010803		
JP 57031613	A2	19820220	JP 1981-92081	19810615
JP 04032052	B4	19920528		
AT 8102665	A	19840715	AT 1981-2665	19810615
AT 377180	B	19850225		
CH 651206	A	19850913	CH 1981-3939	19810615

PRIORITY APPLN. INFO.: US 1980-159973 A2 19800616

AB Protozoa infections in animals, especially coccidiosis in chickens, are prevented or treated by administration of amines, H2NCHMeCH2CH2CHYNH2 in which Y is CH2F, CHF2, or C.tplbond.CH, or amino acids, H2NCZYCO2H in which Y is CH2F, CHF2, CF3, or C.tplbond.CH and Z is H2N(CH2)3, H2NCMe(CH2)2, or H2NCH2CH:CH. The compds. can be given in feed or drinking water. Ornithine dibenzaldimine Me ester [69955-51-7] in THF was bubbled with CHClF2 [75-45-6] in the presence of Li diisopropylamide. The product was partitioned between saturated saline and Et2O, and the purified Et2O extract was refluxed with HCl and further purified to give 2-(difluoromethyl)-2,5-diaminopentanoic acid-HCl [**81645-68-3**]. Granules for adding to poultry drinking water contained 2-(difluoromethl)-2,5-diaminopentanoic acid [70052-12-9] 33.0, corn starch 18.5, lactose 48.2, and Zn stearate 0.3 g. Tests with chickens infected with Eimeria tenella are described.

IT **81645-68-3P**
RL: PREP (Preparation)
(preparation of, for protozoacide)

RN 81645-68-3 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:187316 CAPLUS
DOCUMENT NUMBER: 96:187316
TITLE: Veterinary compositions for inhibiting protozoa development
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Fr. Demande, 45 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2484255	A1	19811218	FR 1981-11733	19810615
FR 2484255	B1	19841214		
SE 8103678	A	19811217	SE 1981-3678	19810611
SE 460517	B	19891023		
SE 460517	C	19900215		
AU 8171654	A1	19811224	AU 1981-71654	19810611
AU 544990	B2	19850627		
ZA 8103953	A	19820630	ZA 1981-3953	19810611
CA 1174603	A1	19840918	CA 1981-379588	19810611
DE 3123295	A1	19820429	DE 1981-3123295	19810612
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IL 63087	A1	19841031	IL 1981-63087	19810612
DE 3153623	C2	19910627	DE 1981-3153623	19810612
BE 889230	A1	19811215	BE 1981-205104	19810615
GB 2078735	A	19820113	GB 1981-18326	19810615
GB 2078735	B2	19850515		
NL 8102863	A	19820118	NL 1981-2863	19810615
NL 194153	B	20010402		
NL 194153	C	20010803		
JP 57031613	A2	19820220	JP 1981-92081	19810615
JP 04032052	B4	19920528		
AT 8102665	A	19840715	AT 1981-2665	19810615
AT 377180	B	19850225		
CH 651206	A	19850913	CH 1981-3939	19810615

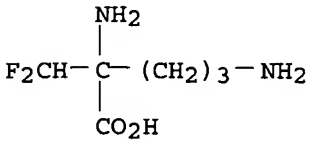
PRIORITY APPLN. INFO.: US 1980-159973 A 19800616

AB α-Substituted amines or α-substituted α-amino acids, e.g. 2-difluoromethyl-2,5-diaminopentanoic acid-HCl (I-HCl) [**81645-68-3**], α-ethynyl-α,δ-diaminovaleric acid [67605-54-3], 1-fluoromethyl-1,4-butanediamine-2HCl [69768-61-2], 1-fluoromethyl-4-methyl-1,4-butanediamine-2HCl [81645-69-4], or 1-ethynyl-4-methyl-1,4-butanediamine [81645-70-7], were prepared and used for inhibiting the development of protozoa, e.g. of the classes Mastigophora and Telosporea. Thus, I, m. 138°, was prepared in 37% yield by treating ornithine dibenzaldimine Me ester [69955-51-7] with a strong base, e.g. Li diisopropylamide, followed by treating the intermediate carbanion with CHClF2 [75-45-6] in THF. Granules were prepared containing I 33, starch 18.5, lactose 48.2, and Zn stearate 0.3 g.

Mice given 2% I solution for 6 days (600 mg I total) survived >30 days following infection with Trypanosoma brucei brucei, as compared to 0 days for infected mice given no treatment.

IT **81645-68-3P**
RL: PREP (Preparation)
(preparation of, for veterinary protozoacide)

RN 81645-68-3 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

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       3259990 PREP/RL
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                 (81645-68-3 (L) PREP/RL)

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             3 81645-68-3
       3626629 PROC/RL
L5           0 81645-68-3/PROC
                 (81645-68-3 (L) PROC/RL)

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                 (81645-68-3 (L) PUR/RL)

=> s l1 full
   REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



FULL SEARCH INITIATED 11:03:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    314 TO ITERATE

100.0% PROCESSED     314 ITERATIONS                          17 ANSWERS
SEARCH TIME: 00.00.01

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L9          12 L8 AND (CYAN? OR NITRILE)

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=> s l8 and hydroly?
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L12         16 L8 AND HYDROLY?

=> s l12 and l9
L13          0 L12 AND L9

=> s l12 and base
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L14          4 L12 AND BASE

=> s l9 and l14
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L17         22 L16 AND PY<2001

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L10  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1997:98548  CAPLUS
DOCUMENT NUMBER:          126:207158
TITLE:                    A cytotoxicity assay for evaluation of candidate
                          anti-Pneumocystis carinii agents
AUTHOR(S):                Cushion, Melanie T.; Chen, Franklin; Kloepfer, Natalie
CORPORATE SOURCE:         Dep. Internal Med., Univ. Cincinnati Coll. Med.,
                          Cincinnati, OH, 45627-0560, USA
SOURCE:                   Antimicrobial Agents and Chemotherapy (1997), 41(2),
                          379-384
                          CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A series of over 60 agents representing several different classes of
     compds. were evaluated for their effects on the ATP pools of Pneumocystis
     carinii populations derived from immunosuppressed rats. A cytotoxicity
     assay based on an ATP-driven bioluminescent reaction was used to determine the
     concentration of agent which decreased the P. carinii ATP pools by 50% vs.
     untreated controls (IC50). A ranking system based on the IC50 values was
     devised for comparison of relative responses among the compds. evaluated
     in the cytotoxic assay and for comparison to in vivo efficacy. With few
     exceptions, there was a strong correlation between results from the ATP
     assay and the performance of the compound in vivo. Antibiotics, with the
     exception of trimethoprim-sulfamethoxazole (TMP-SMX), were ineffective at
     reducing the ATP pools and were not active, clin. or in the rat
     model of P. carinii pneumonia. Likewise, other agents not expected to be
     effective, e.g., antiviral compds., did not show activity. Standard anti-P.
     carinii compds., e.g., TMP-SMX, pentamidine, and dapsone, dramatically
     reduced ATP levels. Analogs of the quinone and topoisomerase
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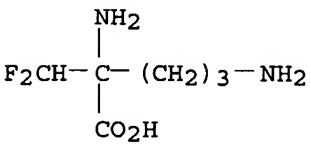
inhibitor groups were shown to **reduce** ATP concns. and hold promise for further in vivo investigation. The cytotoxicity assay provides a rapid assessment of response, does not rely on replicating organisms, and should be useful for assessment of structure-function relationships.

IT **70052-12-9**, DFMO
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxicity assay for evaluation of candidate anti-Pneumocystis carinii agents)

RN 70052-12-9 CAPLUS

CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L17 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:60013 CAPLUS

DOCUMENT NUMBER: 130:231817

TITLE: Plasma analysis of α-difluoromethylornithine using pre-column derivatization with naphthalene-2,3-dicarboxaldehyde/CN and multidimensional chromatography

AUTHOR(S): Kilkenny, Mary L.; Slavik, Milan; Riley, Christopher M.; Stobaugh, John F.

CORPORATE SOURCE: Hoechst Marion Roussel Incorporated, Kansas City, MO, 64134-0627, USA

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (**1998**), 17(6,7), 1205-1213
CODEN: JPBADA; ISSN: 0731-7085

PUBLISHER: Elsevier Science B.V.

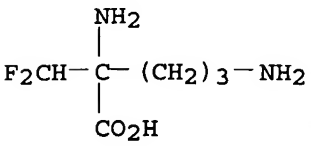
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A procedure for the plasma anal. of a-difluoromethylornithine (DFMO) has been developed that utilizes pre-column derivatization with naphthalene-2,3-dicarboxaldehyde/**cyanide** (NDA/CN) in pH 9.2 borate buffer. Selective derivatization of δ-amine of DFMO followed by quenching of the reaction results in the formation of a **cyanobenz**[f]isoindole (CBI) derivative that is stable for 24 h. Plasma was prepared for derivatization by a single step procedure which resulted in an ultrafiltrate compatible with derivatization and anal. The DFMO derivative (CBI-DFMO) was separated from plasma interferences by multidimensional chromatog. with an anal. time of 28 min. The response for DFMO in plasma was linear over the range of 2.1+10-8-2.1+10-6 M after derivatization. This procedure encompasses a useful linear range and offers the advantages of minimal sample preparation and production of a stable fluorophor.

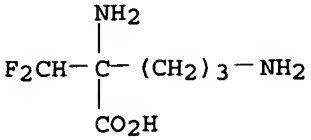
IT **70052-12-9**, α-Difluoromethylornithine
RL: ANT (Analyte); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent)
(plasma anal. of α-difluoromethylornithine using pre-column

derivatization with naphthalene-2,3-dicarboxaldehyde/CN and multidimensional chromatog.)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



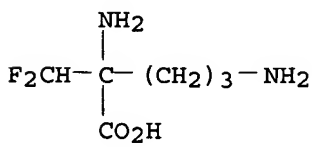
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:98548 CAPLUS
DOCUMENT NUMBER: 126:207158
TITLE: A cytotoxicity assay for evaluation of candidate anti-Pneumocystis carinii agents
AUTHOR(S): Cushion, Melanie T.; Chen, Franklin; Kloepfer, Natalie
CORPORATE SOURCE: Dep. Internal Med., Univ. Cincinnati Coll. Med., Cincinnati, OH, 45627-0560, USA
SOURCE: Antimicrobial Agents and Chemotherapy (**1997**), 41(2), 379-384
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of over 60 agents representing several different classes of compds. were evaluated for their effects on the ATP pools of Pneumocystis carinii populations derived from immunosuppressed rats. A cytotoxicity assay based on an ATP-driven bioluminescent reaction was used to determine the concentration of agent which decreased the P. carinii ATP pools by 50% vs. untreated controls (IC50). A ranking system based on the IC50 values was devised for comparison of relative responses among the compds. evaluated in the cytotoxic assay and for comparison to in vivo efficacy. With few exceptions, there was a strong correlation between results from the ATP assay and the performance of the compound in vivo. Antibiotics, with the exception of trimethoprim-sulfamethoxazole (TMP-SMX), were ineffective at reducing the ATP pools and were not active, clin. or in the rat model of P. carinii pneumonia. Likewise, other agents not expected to be effective, e.g., antiviral compds., did not show activity. Standard anti-P. carinii compds., e.g., TMP-SMX, pentamidine, and dapsone, dramatically reduced ATP levels. Analogs of the quinone and topoisomerase inhibitor groups were shown to reduce ATP concns. and hold promise for further in vivo investigation. The cytotoxicity assay provides a rapid assessment of response, does not rely on replicating organisms, and should be useful for assessment of structure-function relationships.
IT **70052-12-9**, DFMO
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxicity assay for evaluation of candidate anti-Pneumocystis carinii agents)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:949690 CAPLUS
DOCUMENT NUMBER: 124:25085
TITLE: Determination of α-difluoromethylornithine in blood by microdialysis sampling and capillary electrophoresis with UV detection
AUTHOR(S): Hu, Tao; Zuo, Hong; Riley, Christopher M.; Stobaugh, John F.; Lunte, Susan M.
CORPORATE SOURCE: Center for Bioanalytical Research, University of Kansas, 2095 Constant Avenue, Lawrence, KS, 66047, USA
SOURCE: Journal of Chromatography, A (**1995**), 716(1 + 2), 381-8
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A procedure is described for the anal. of α-difluoromethylornithine (DFMO), an anti-cancer agent, in plasma microdialysis (MD) samples. DFMO has been shown to be effective alone or in combination with other agents in the treatment of several cancers. Precolumn derivatization of DFMO with naphthalene-2,3-dicarboxaldehyde-**cyanide** (NDA-CN) in pH 10.0 borate buffer results in the rapid formation of a stable mono-derivatized product (N-substituted 1-**cyanobenz**[f]isoindole, CBI), which is UV active. An anal. method has been developed to sep. CBI-DFMO from NDA-CN derivatization products of 20 standard amino acids using capillary electrophoresis (CE). This method is then employed for the determination of DFMO in plasma microdialysis samples. Separation of DFMO from other components in the dialyzate was achieved within 20 min. The response for DFMO in Ringer's solution was linear over the range of 1.2·10-6 to 1.6·10-4 M after derivatization. The detection limit of DFMO in the plasma dialyzate is 5 μM using UV detection at 254 nm. This method has been proven to have adequate sensitivity for quantitation of DFMO in i.v. microdialyzate samples and has been successfully applied to monitoring the pharmacokinetics of DFMO by CE-UV.
IT **70052-12-9**, α-Difluoromethylornithine
RL: ANT (Analyte); ANST (Analytical study)
(determination of α-difluoromethylornithine in blood by microdialysis sampling and capillary electrophoresis with UV detection)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



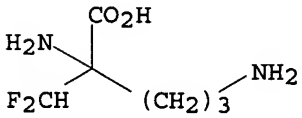
L17 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:603794 CAPLUS
DOCUMENT NUMBER: 119:203794

TITLE: Synthesis of amino acid and related compounds. Part 40. Convenient synthesis of α-difluoromethylornithine
AUTHOR(S): Seki, Masahiko; Suzuki, Mamoru; Matsumoto, Kazuo
CORPORATE SOURCE: Res. Lab. Appl. Biochem., Tanabe Seiyaku Co., Ltd., Osaka, 532, Japan
SOURCE: Bioscience, Biotechnology, and Biochemistry (**1993**), 57(6), 1024-5
CODEN: BBBIEJ; ISSN: 0916-8451
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:203794

AB The title compound, H2N(CH2)3C(CHF2)(NH2)CO2H, was prepared in 5 steps in 10% overall yield from H-L-Orn-OMe.2HCl. Key diisocyanato intermediate CN(CH2)3CH(NC)CO2Me was prepared via the diformyl derivative and alkylated with ClCHF2, followed by acid **hydrolysis**.

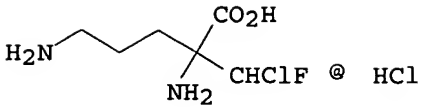
IT **68278-23-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via alkylation of diisocyanatopentanoate with chlorodifluoromethane)

RN 68278-23-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L17 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:572003 CAPLUS
DOCUMENT NUMBER: 117:172003
TITLE: Synthesis and inhibitory properties of α-(chlorofluoromethyl) α-amino acids, a novel class of irreversible inactivators of decarboxylases
AUTHOR(S): Schirlin, D.; Ducep, J. B.; Baltzer, S.; Bey, P.; Piriou, F.; Wagner, J.; Hornsperger, J. M.; Heydt, J. G.; Jung, M. J.; et al.
CORPORATE SOURCE: Marion Merrell Dow Res. Inst., Strasbourg, 67009, Fr.
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (**1992**), (8), 1053-64
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:172003
GI



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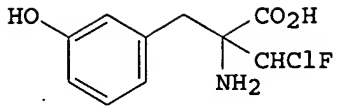
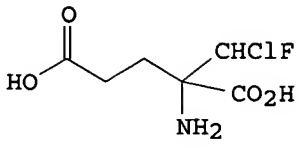


II



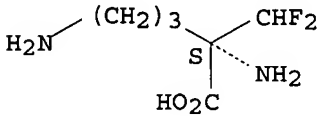
III

AB The synthesis of α-(chlorofluoromethyl)ornithine I, -m-tyrosine II and -glutamic acid III is described. Separation of diastereoisomers and relative configuration assignment by x-ray anal. are reported. Assignment of absolute configuration of the four enantiomers of I is also described. The inhibitory properties against ornithine decarboxylase, aromatic amino acid decarboxylase and glutamate decarboxylase are reported in terms of diastereoselectivity (II and III) or enantioselectivity (I).

IT **66640-93-5 69955-42-6 70050-55-4**
103957-16-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(ornithine decarboxylase-inhibiting activity of)

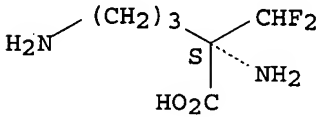
RN 66640-93-5 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

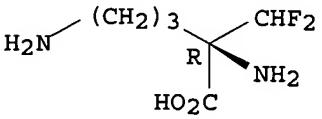
Absolute stereochemistry. Rotation (-).



● HCl

RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

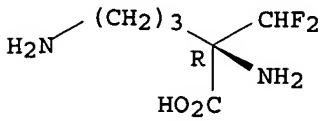
Absolute stereochemistry. Rotation (+).



● HCl

RN 103957-16-0 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

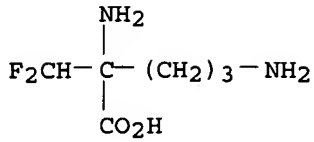


L17 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:156652 CAPLUS
DOCUMENT NUMBER: 114:156652
TITLE: Antitrypanosomal effects of polyamine biosynthesis inhibitors correlate with increases in Trypanosoma brucei brucei S-adenosyl-L-methionine
AUTHOR(S): Byers, Timothy L.; Bush, Tammy L.; McCann, Peter P.; Bitonti, Alan J.
CORPORATE SOURCE: Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Biochemical Journal (**1991**), 274(2), 527-33
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

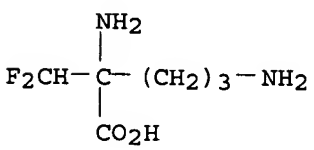
AB Administration of 5'-{[(Z)-4-amino-2-butenyl]methylamino}-5'-deoxyadenosine (MDL 73811), an enzyme-activated irreversible inhibitor of S-adenosyl-L-methionine decarboxylase (AdoMetDC; EC 4.1.1.50), a key enzyme in the synthesis of spermidine, to T. brucei brucei-infected rats resulted in a 70% decrease in parasitemia within 1 h and a complete disappearance of parasites by 5 h. The reduction in parasitemia was accompanied by complete inhibition of AdoMetDC activity in 10 min after injection of MDL 73811; inhibition was sustained for at least 4 h. Polyamine levels in trypanosomes were unaffected during the first 1 h in which the marked decrease in parasitemia was observed, but parasite AdoMet levels increased 20-fold within this time. In contrast, exposure of cultured mammalian cells to MDL 73811 resulted in only a 1.5-2-fold increase in AdoMet levels over a 6 h time course. Expts. with inhibitors of ornithine decarboxylase (ODC) also suggested that the increased AdoMet levels might be an important factor for antitrypanosomal efficacy. Trypanosomes taken from rats treated for 36 h with eflornithine, an inhibitor of ODC, were depleted of putrescine and had markedly decreased spermidine levels. These organisms also had <10% of control AdoMetDC activity, and had elevated decarboxy AdoMet (>4000-fold) and AdoMet (up to 50-fold) levels. The Me ester of α-monofluromethyl-3,4-dehydro-ornithine (Δ-MFMO-CH3), which cures murine T. brucei brucei infections, and the Et ester analog of this compound (Δ-MFMO-C2H5), which does not cure this infection, become ODC inhibitors upon **hydrolysis** and thus were tested for their effects on trypanosomal polyamines, AdoMet and decarboxy AdoMet levels. Although both esters of Δ-MFMO depleted trypanosomal polyamines, AdoMet and decarboxy AdoMet levels were elevated in T. brucei brucei from infected mice treated with Δ-MFMO-CH3 but not in parasites from mice treated with the Δ-MFMO-C2H5. These data suggest that inhibition of AdoMetDC, either directly with MDL 73811 or indirectly with inhibitors of ODC, apparently leads to a trypanosome-specific elevation of AdoMet. It is possible that major changes in AdoMet, rather than changes in polyamines, may be responsible for the antitrypanosomal effects of these drugs.

IT **70052-12-9**, Eflornithine
RL: PRP (Properties)
(antitrypanosomal effects of, Trypanosoma brucei brucei adenosylmethionine response to)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:607070 CAPLUS
DOCUMENT NUMBER: 109:207070
TITLE: DL-α-Difluoromethyl[3,4-3H]arginine metabolism in tobacco and mammalian cells. Inhibition of ornithine decarboxylase activity after arginase-mediated **hydrolysis** of DL-α-difluoromethylarginine to DL-α-difluoromethylornithine
AUTHOR(S): Slocum, Robert D.; Bitonti, Alan J.; McCann, Peter P.; Feirer, Russell P.
CORPORATE SOURCE: Dep. Biol., Williams Coll., Williamstown, MA, 01267, USA
SOURCE: Biochemical Journal (**1988**), 255(1), 197-202
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DL-α-Difluoromethylarginine (DFMA) is an enzyme-activated irreversible inhibitor of arginine decarboxylase (ADC) in vitro. DFMA has also been shown to inhibit ADC activities in a variety of plants and bacteria in vivo. However, the specificity of this inhibitor for ADC in tobacco ovary tissues was questioned, since ornithine decarboxylase (ODC) activity was strongly inhibited as well. [3,4-3H2]DFMA is metabolized to DL-α-difluoromethyl[3,4-3H2]ornithine ([3,4-3H2]DFMO), the analogous mechanism-based inhibitor of ODC, by tobacco tissues in vivo. Both tobacco and mammalian (mouse and bovine) arginases (EC 3.5.3.1) **hydrolyze** DFMA to DFMO in vitro, suggesting a role for this enzyme in mediating the indirect inhibition of ODC by DFMA in tobacco. Thus, DFMA may have other effects, in addition to the inhibition of ADC, in tissues containing high arginase activities. The recent development of potent agmatine-based ADC inhibitors should permit selective inhibition of ADC, rather than ODC, in such tissues, since agmatine is not a substrate for arginase.
IT **70052-12-9P**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, from difluoromethylarginine in tobacco ovary and mammal liver)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



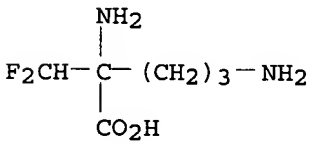
L17 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:466216 CAPLUS
DOCUMENT NUMBER: 109:66216
TITLE: Validity of short-term examination for antipromoters

of bladder carcinogenesis
AUTHOR(S): Kakizoe, Tadao; Takai, Kazuhiro; Tobisu, Kenichi; Ohtani, Mikinobu; Sato, Shigeaki
CORPORATE SOURCE: Urol. Div., Natl. Cancer Cent. Hosp., Tokyo, 104, Japan
SOURCE: Japanese Journal of Cancer Research (**1988**), 79(2), 231-5.
CODEN: JJCREP; ISSN: 0910-5050
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various compds. were screened for antipromoter activity in bladder carcinogenesis in rats with a view to using them clin. to inhibit postoperative intravesical ectopic tumor growth of superficial papillary bladder cancer. Their inhibitions of the effect of Na saccharin in maintaining increased agglutinability of bladder cells by Con A were examined in 4-wk tests. The compds. found to inhibit the effect of saccharin were α-tocopherol, ascorbic acid, aspirin, all-trans aromatic retinoid, α-difluoromethylornithine, sodium **cyanate** and p,p'-diaminodiphenylmethane. Considering the toxicities of some of these chems., ascorbic acid and α-difluoromethylornithine were concluded to be the most promising for future clin. trials.

IT **70052-12-9**, α-Difluoromethylornithine
RL: PRP (Properties)
(antipromoter effects of, on bladder carcinogenesis)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



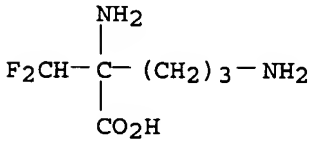
L17 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:146047 CAPLUS
DOCUMENT NUMBER: 108:146047
TITLE: Putrescine derivatives as substrates of spermidine synthase
AUTHOR(S): Sarhan, S.; Dezeure, F.; Seiler, N.
CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, 67084, Fr.
SOURCE: International Journal of Biochemistry (**1987**), 19(11), 1037-47
CODEN: IJBOBV; ISSN: 0020-711X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Derivs. of 1,4-butanediamine (putrescine) were studied in vitro and in vivo as potential substrates of spermidine synthase. Substituents in the 1-position decreased the reaction rate by steric hindrance, and in the case of electron-withdrawing groups there was an addition decrease due to the lowered basicity of the vicinal amino group. Substituents in the 2-position were tolerated; under saturating conditions, reaction rates were comparable to those of putrescine. Compds. which were identified as substrates of spermidine synthase in vitro formed derivs. of spermidine and spermine in vivo. However, compds. such as 1-methylputrescine formed in vivo only a spermidine derivative, because the 2nd aminopropylation was sterically hindered by the substituent on the C atom next to the amino group. The administration of 2-hydroxyputrescine to α-difluoromethylornithine-pretreated chick embryos produced spermidine and spermine analogs in amts. exceeding spermidine and spermine formation from putrescine under comparable conditions. Since the concentration of 2-hydroxyputrescine in the embryo was higher than that of putrescine and

all other putrescine analogs, uptake of the polyamine precursor from the yolk may be rate-limiting. Three days after administration of 5 mM α-difluoromethylornithine, there was a near-to-complete arrest of embryonal growth. A series of diamines supported growth under these conditions, even if they were not substrates of spermidine synthase. The survival of chick embryos was, however, only supported if the diamines were capable of forming significant amts. of spermidine and spermine analogs.

IT **70052-12-9**, DL-α-Difluoromethylornithine
RL: BIOL (Biological study)
(chick embryo response to, putrescine analogs effect on)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:103892 CAPLUS
DOCUMENT NUMBER: 100:103892
TITLE: 2-(Difluoromethyl)-2,5-diaminopentanoic acid
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 53,937, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4413141	A	19831101	US 1982-419347	19820917 <--
US 4438270	A	19840320	US 1982-392051	19820625 <--
US 4496588	A	19850129	US 1983-487243	19830428 <--
US 4560795	A	19851224	US 1984-577116	19840206 <--
US 5614557	A	19970325	US 1995-403531	19950314 <--
PRIORITY APPLN. INFO.:			US 1977-814765	A1 19770711
			US 1979-53937	A2 19790702
			US 1979-28757	B1 19790410
			US 1979-28758	A1 19790410
			US 1980-204749	B2 19801107
			US 1981-262834	B1 19810512
			US 1982-382265	B3 19820526
			US 1982-392051	A3 19820625
			US 1982-373198	A1 19820929
			US 1984-639977	B1 19840810
			US 1987-110639	B1 19871015
			US 1988-228789	B1 19880804
			US 1989-334733	B1 19890406
			US 1989-431685	B1 19891103
			US 1990-534008	B1 19900601
			US 1991-759633	B1 19910912
			US 1992-874989	B1 19920424
			US 1993-2521	B1 19930111
			US 1993-137397	B1 19931014
			US 1994-284706	B1 19940802

OTHER SOURCE(S): CASREACT 100:103892

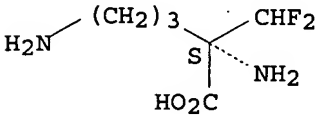
AB The title compound (I) was prepared as an ornithine decarboxylase inhibitor (no data). Thus, solns. of (Me2CH)2NH and dibenzylideneornithine Me ester in THF were added to BuLi in hexane at -78° and ClCHF2 was bubbled in at 40-50° for 3 h to give I.HCl. The product could be resolved via its (-)-binaphthylphosphate salt.

IT **66640-93-5P 69955-42-6P 70050-55-4P**
81645-68-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 66640-93-5 CAPLUS

CN L-Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)

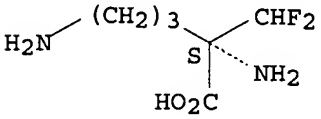
Absolute stereochemistry. Rotation (-).



RN 69955-42-6 CAPLUS

CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

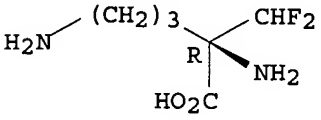


● HCl

RN 70050-55-4 CAPLUS

CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

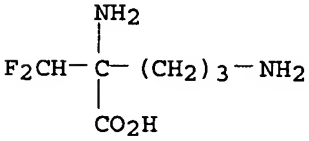
Absolute stereochemistry. Rotation (+).



● HCl

RN 81645-68-3 CAPLUS

CN Ornithine, 2-(difluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L17 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:581486 CAPLUS
DOCUMENT NUMBER: 99:181486
TITLE: Inhibiting the growth of protozoa
INVENTOR(S): Sjoerdsma, Albert; McCann, Peter P.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 159,973, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

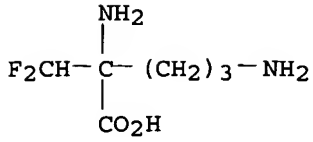
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4399151	A	19830816	US 1981-262275	19810511 <--
SE 8103678	A	19811217	SE 1981-3678	19810611 <--
SE 460517	B	19891023		
SE 460517	C	19900215		
AU 8171654	A1	19811224	AU 1981-71654	19810611 <--
AU 544990	B2	19850627		
ZA 8103953	A	19820630	ZA 1981-3953	19810611 <--
CA 1174603	A1	19840918	CA 1981-379588	19810611 <--
DE 3123295	A1	19820429	DE 1981-3123295	19810612 <--
DE 3123295	C2	19900712		
IL 63087	A1	19841031	IL 1981-63087	19810612 <--
DE 3153623	C2	19910627	DE 1981-3153623	19810612 <--
BE 889230	A1	19811215	BE 1981-205104	19810615 <--
GB 2078735	A	19820113	GB 1981-18326	19810615 <--
GB 2078735	B2	19850515		
NL 8102863	A	19820118	NL 1981-2863	19810615 <--
NL 194153	B	20010402		
NL 194153	C	20010803		
JP 57031613	A2	19820220	JP 1981-92081	19810615 <--
JP 04032052	B4	19920528		
AT 8102665	A	19840715	AT 1981-2665	19810615 <--
AT 377180	B	19850225		
CH 651206	A	19850913	CH 1981-3939	19810615 <--

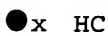
PRIORITY APPLN. INFO.: US 1980-159973 A2 19800616

AB Protozoa infections in animals, especially coccidiosis in chickens, are prevented or treated by administration of amines, H2NCHMeCH2CH2CHYNH2 in which Y is CH2F, CHF2, or C.tplbond.CH, or amino acids, H2NCZYCO2H in which Y is CH2F, CHF2, CF3, or C.tplbond.CH and Z is H2N(CH2)3, H2NCMe(CH2)2, or H2NCH2CH:CH. The compds. can be given in feed or drinking water. Ornithine dibenzaldimine Me ester [69955-51-7] in THF was bubbled with CHClF2 [75-45-6] in the presence of Li diisopropylamide. The product was partitioned between saturated saline and Et2O, and the purified Et2O extract was refluxed with HCl and further purified to give 2-(difluoromethyl)-2,5-diaminopentanoic acid-HCl [**81645-68-3**]. Granules for adding to poultry drinking water contained 2-(difluoromethl)-2,5-diaminopentanoic acid [**70052-12-9**] 33.0, corn starch 18.5, lactose 48.2, and Zn stearate 0.3 g. Tests with chickens infected with Eimeria tenella are described.

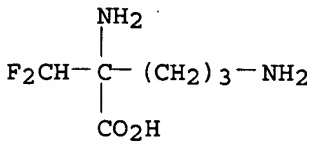
IT **81645-68-3P**
RL: PREP (Preparation)
(preparation of, for protozoacide)

RN 81645-68-3 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, hydrochloride (9CI) (CA INDEX NAME)

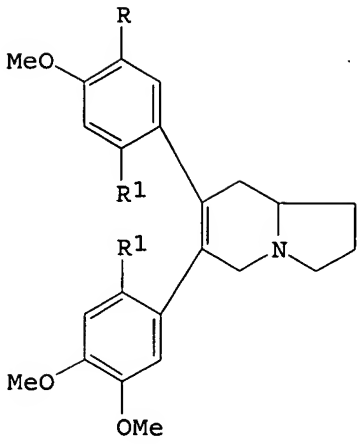




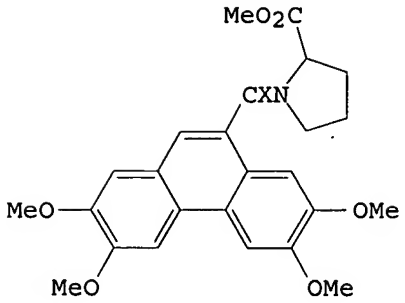
IT **70052-12-9**
RL: BIOL (Biological study)
(protozoacidal composition containing)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



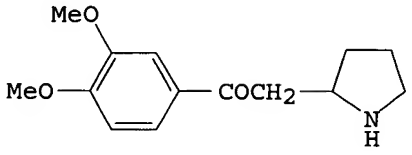
L17 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:72508 CAPLUS
DOCUMENT NUMBER: 98:72508
TITLE: Phenanthroindolizidine and related alkaloids: synthesis of tylophorine, septicine, and deoxytylophorinine
AUTHOR(S): Cragg, John E.; Herbert, Richard B.; Jackson, Frederick B.; Moody, Christopher J.; Nicolson, Ian T.
CORPORATE SOURCE: Dep. Org. Chem., Univ. Leeds, Leeds, LS2 9JT, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (**1982**), (10), 2477-85
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 98:72508
GI



I



III



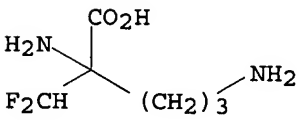
IV

AB Two syntheses of tylophorine (I; R = OMe, R12 = bond) (II) was described. Successive treatment of the ester amide III (X = O) with Et3O.BF4 and NaBH4 gave III (X = H2), which underwent sequential **hydrolysis**, acid-catalyzed ring closure, and Clemmenson reduction to give II. Alternatively, condensation of 3,4-(MeO)2C6H3COCH2CO2H with 1-pyrroline gave the ketone IV; IV was condensed with 3,4-(MeO)2C6H3CH2CHO in C6H6 to give an enamine which underwent cyclization and dehydration in MeOH followed by NaBH4 reduction to give septicine (I; R = OMe, R1 = H) (V). Oxidation of V with Tl(O2CCF3)3 gave II. Deoxytylophorinine (I; R = H, R12 = bond) was similarly prepared

IT **68278-23-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of, by NBS)

RN 68278-23-9 CAPLUS

CN Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

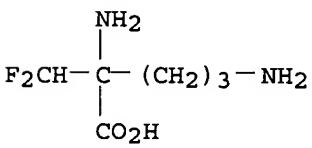
L17 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:65102 CAPLUS
DOCUMENT NUMBER: 98:65102
TITLE: Biological properties of N4-spermidine derivatives and their potential in anticancer chemotherapy
AUTHOR(S): Porter, Carl W.; Bergeron, Raymond J.; Stolowich, Neal J.
CORPORATE SOURCE: Grace Cancer Drug Cent., Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
SOURCE: Cancer Research (**1982**), 42(10), 4072-8
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Various spermidine (SPD) derivs. and the anticancer agent methylglyoxal-bis(guanylhydrazone) [459-86-9] were studied for their ability to affect the growth of cultured L1210 leukemia cells, to inhibit SPD uptake into L1210 cells, and to substitute for SPD in biol. function(s) related to cell proliferation. The SPD derivs. included a series in which the central amine of SPD, norspermidine [56-18-8] or homospermidine [4427-76-3], was benzyl substituted and another series in which the terminal amines of the same triamines were butoxycarbonyl substituted. In addition, the derivs., N4-benzylspermidine **nitrile** [75802-65-2] and N1,N8-dihydroxybenzoylspermidine [54135-84-1] were studied. Only the latter compound showed significant cytotoxicity to L1210 cells (50% growth-ID, 10 μM), and this was probably attributable to its iron-chelating properties. SPD uptake by L1210 cells was partially characterized (Km 2.0 mM; Vmax 177 pmol/mg/min) and found to be dependent on cellular energy production Inhibition of SPD uptake by compds. with derivatized central amines was of the competitive type while that by compds. with derivatized terminal amines was too weak to be accurately characterized. Specificity of uptake was found to be dependent on the availability of the primary amines and to a lesser extent on aliphatic chain length. N4-Benzylspermidine competed well with [3H]SPD for uptake (Ki 36 μM) and was slightly more effective than methylglyoxal-bis(guanylhydrazone)(Ki 53 μM) in this regard. By contrast, N1,N8-bis(butoxycarbonyl)spermidine [83392-10-3] competed very poorly with [3H]SPD for uptake (Ki μM). In the case of N4-benzylspermidine, cellular uptake was confirmed by high-pressure liquid chromatog. of cell exts. Pretreatment of cells for 24 h with the inhibitor of SPD biosynthesis, α-difluoromethylornithine [**70052-12-9**], enhanced uptake of N4-benzylspermidine [73038-05-8] by about 3-fold. None of the compds. were capable of substituting for SPD biol. as indicated by their inability to prevent cytostasis induced by α-difluoromethylornithine. The uptake data, in particular, indicate good potential for N4-spermidine derivs. as vector mols. for chemical moieties having biol. activity. In theory, they should prove functional as anticancer agents, and their activity could be augmented by pretreatment with α-difluoromethylornithine to increase their uptake.

IT **70052-12-9**
RL: BIOL (Biological study)
(spermidine derivative uptake response to, neoplasm inhibition in relation to)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:544373 CAPLUS
DOCUMENT NUMBER: 97:144373
TITLE: Compound for treating benign prostatic hypertrophy
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., USA
SOURCE: U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 28,739, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

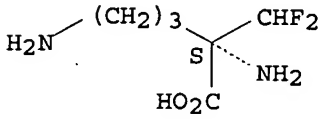
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4330559	A	19820518	US 1981-231072	19810203 <--
US 4496588	A	19850129	US 1983-487243	19830428 <--
US 4560795	A	19851224	US 1984-577116	19840206 <--
US 5614557	A	19970325	US 1995-403531	19950314 <--
PRIORITY APPLN. INFO.:			US 1977-814765 A2	19770711
			US 1979-28739 A2	19790410
			US 1979-28757 B1	19790410
			US 1979-28758 A1	19790410
			US 1979-53937 A1	19790702
			US 1980-204749 B2	19801107
			US 1981-262834 B1	19810512
			US 1982-382265 B3	19820526
			US 1982-392051 A3	19820625
			US 1982-373198 A1	19820929
			US 1984-639977 B1	19840810
			US 1987-110639 B1	19871015
			US 1988-228789 B1	19880804
			US 1989-334733 B1	19890406
			US 1989-431685 B1	19891103
			US 1990-534008 B1	19900601
			US 1991-759633 B1	19910912
			US 1992-874989 B1	19920424
			US 1993-2521 B1	19930111
			US 1993-137397 B1	19931014
			US 1994-284706 B1	19940802

AB R1NH(CH2)3CR3(NHR2)COR [R = OH, C1-8 alkoxy, (un)substituted amide, etc.; R1, R2 = H, C1-4 alkoxycarbonyl, etc.; R3 = CH2F, CHF2, CF3] were prepared for treatment of benign prostate hypertrophy. Thus, L-ornithine was converted into the Me ester-HCl, protected with BzH, difluoromethylated with BuLi-CHF2Cl, and the product **hydrolyzed** to give H2N(CH2)3C(CHF2)(NH2)CO2H.

IT **69955-42-6P 70050-55-4P 70052-12-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

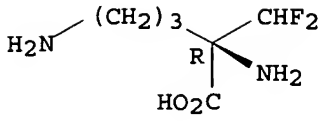
Absolute stereochemistry. Rotation (-).



● HCl

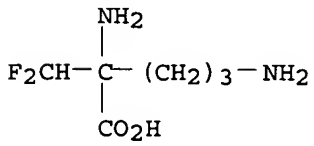
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:205402 CAPLUS
DOCUMENT NUMBER: 96:205402
TITLE: Controlling fertility in mammals
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 58,476.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

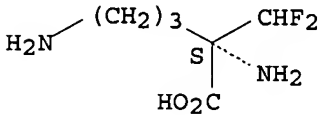
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 4309442	A	19820105	US 1980-212473	19801203	<--
US 4496588	A	19850129	US 1983-487243	19830428	<--
US 4560795	A	19851224	US 1984-577116	19840206	<--
US 5614557	A	19970325	US 1995-403531	19950314	<--
PRIORITY APPLN. INFO.:			US 1977-814765	A2 19770711	
			US 1979-58476	A2 19790718	
			US 1979-28757	B1 19790410	
			US 1979-28758	A1 19790410	
			US 1979-53937	A1 19790702	
			US 1980-204749	B2 19801107	
			US 1981-262834	B1 19810512	
			US 1982-382265	B3 19820526	
			US 1982-392051	A3 19820625	
			US 1982-373198	A1 19820929	
			US 1984-639977	B1 19840810	
			US 1987-110639	B1 19871015	
			US 1988-228789	B1 19880804	
			US 1989-334733	B1 19890406	
			US 1989-431685	B1 19891103	
			US 1990-534008	B1 19900601	
			US 1991-759633	B1 19910912	
			US 1992-874989	B1 19920424	
			US 1993-2521	B1 19930111	
			US 1993-137397	B1 19931014	
			US 1994-284706	B1 19940802	

AB Compns. for gestation prevention in mammals contain α-(halomethyl)ornithine derivs. or their salts and can be administered in

various ways depending upon the mammal to be treated. The compds. may be used to control rodent and other mammal populations. Thus, to 15 L THF cooled to -80° is added 2.82 L iso-Pr2NH under N, and then 12 L of 15% BuLi in hexane at a rate to maintain the temperature at -75 to -80°, followed by dibenzaldimineornithine Me ester [69955-51-7] in 15 L THF; the temperature is gradually increased to 35-40° and maintained for 1 h, N is replaced by ClF2CH [75-45-6], 20 L saturated NaCl and 75 L iso-Pr2O are added, the organic layer is separated, extracted, the exts. are combined, washed with saturated NaCl, the filtrate is evaporated to an oil, the oil **hydrolyzed** with 30 L 1N HCl at room temperature for 3 h, extracted with CHCl3, the residue diluted with 6 L H2O, adjusted to pH 3.3, the mixture warmed, filtered, washed, and recrystd. to give 2,5-diamino-2-(difluoromethyl)pentanoic acid (I) **[67037-37-0]**. A batch for 1000 tablets for oral use was formulated with I 500, CaHPO4 250, Me cellulose 6.5, talc 20, and Ca stearate 2.5 g. The fertility inhibiting effect of I was demonstrated in female mice.

IT **69955-42-6P 70050-55-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

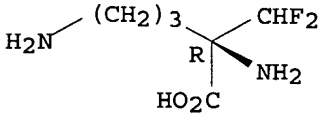
Absolute stereochemistry. Rotation (-).



● HCl

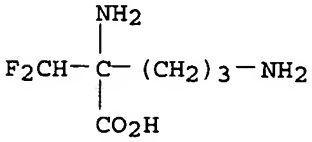
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

IT **70052-12-9P**
RL: PREP (Preparation)
(preparation of, for abortifacient formulations)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



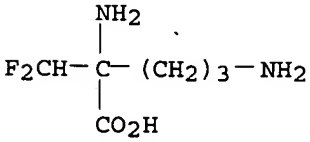
L17 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:503311 CAPLUS
DOCUMENT NUMBER: 95:103311
TITLE: Pharmaceutical composition containing a halomethyl derivative of an α-amino acid useful in retarding the growth of tumors
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: Belg., 53 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 881209	A1	19800516	BE 1980-199012	19800117 <--
US 5614557	A	19970325	US 1995-403531	19950314 <--
PRIORITY APPLN. INFO.:			US 1979-28757 A	19790410
			US 1977-814765 B2	19770711
			US 1980-204749 B2	19801107
			US 1981-262834 B1	19810512
			US 1982-382265 B3	19820526
			US 1984-639977 B1	19840810
			US 1987-110639 B1	19871015
			US 1988-228789 B1	19880804
			US 1989-334733 B1	19890406
			US 1989-431685 B1	19891103
			US 1990-534008 B1	19900601
			US 1991-759633 B1	19910912
			US 1992-874989 B1	19920424
			US 1993-2521 B1	19930111
			US 1993-137397 B1	19931014
			US 1994-284706 B1	19940802

AB The title compns. were prepared containing α-amino acid halomethyl derivs. ZYC(NHR)COR1, e.g. α,δ-diamino-α-difluoromethylvaleric acid (I) [**70052-12-9**] or α-amino-α-fluoromethyl-δ-guanidinovaleric acid [73800-88-1]. These active components inhibited decarboxylases implicated in the formation of polyamines which are associated with normal and neoplastic growth. These derivs. were prepared by treating ornithine or lysine ester derivs. having protected NH2 groups with a strong **base** to form the intermediate carbanion followed by reacting the product with the appropriate halomethyl halo alkylation agent and **hydrolyzing**. Lactams of these compds. were prepared by treating the amino acid esters with an appropiate **base**. A gelatin capsule composition was prepared containing I 200, talc 5, and lactose 10 mg. These compns. were also obtained as tablets or i.m. injections.

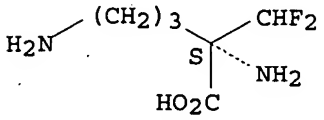
IT **70052-12-9**
RL: BIOL (Biological study)
(neoplasm inhibitor pharmaceuticals containing)

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



IT **69955-42-6P 70050-55-4P 70052-12-9P**
RL: PREP (Preparation)
(preparation of, for neoplasm inhibitor compns.)
RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

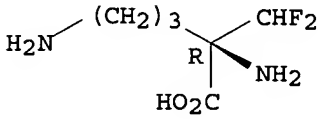
Absolute stereochemistry. Rotation (-).



● HCl

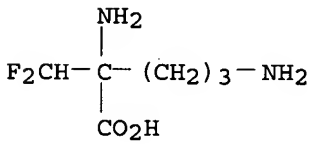
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:503310 CAPLUS
DOCUMENT NUMBER: 95:103310
TITLE: Pharmaceutical composition containing a halomethyl derivative of an α-amino acid useful in the treatment of psoriasis
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: Belg., 53 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 881208	A1	19800516	BE 1980-199011	19800117 <--
US 4496588	A	19850129	US 1983-487243	19830428 <--

PRIORITY APPLN. INFO.: US 1979-28758 A 19790410
US 1977-814765 A2 19770711
US 1982-373198 A1 19820929

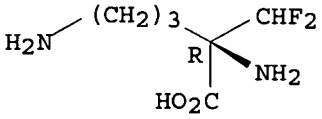
AB The title compns. were prepared containing α-amino acid halomethyl derivs. ZYC(NHR)COR1, e.g. α,δ-diamino-α-difluoromethylvaleric acid (I) [**70052-12-9**], or α-amino-α-fluoromethyl-δ-guanidinovaleric acid [73800-88-1]. These amino acids derivs. are inhibitors of decarboxylases implicated in the formation of polyamines in psoriasis patients. The compds. were prepared by treating ornithine or lysine ester derivs. having protected NH2 groups with a strong **base** to form the intermediate carbanion followed by reacting the product with the appropriate halomethyl halo alkylating agent and **hydrolyzing**. Lactams of these compds. were prepared by treating the amino acid esters with an appropiate **base**. A capsule formulation was prepared containing I 200, talc 5, and lactose 10 mg.

IT **70050-55-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzyloxycarbonylation of)

RN 70050-55-4 CAPLUS

CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

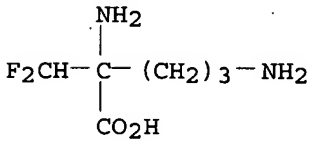


● HCl

IT **70052-12-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing, for psoriasis treatment)

RN 70052-12-9 CAPLUS

CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)

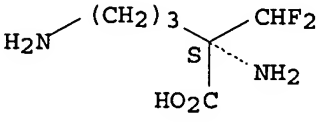


IT **69955-42-6P 70050-55-4P 70052-12-9P**
RL: PREP (Preparation)
(preparation of, for pharmaceuticals for psoriasis treatment)

RN 69955-42-6 CAPLUS

CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

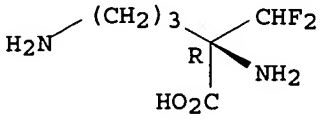
Absolute stereochemistry. Rotation (-).



● HCl

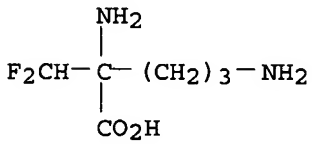
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

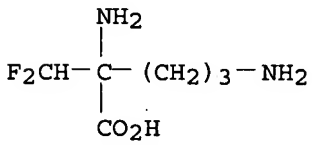


● HCl

RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



IT **70052-12-9**
RL: BIOL (Biological study)
(psoriasis treatment by composition containing)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



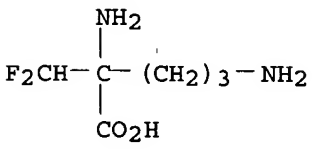
L17 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:145343 CAPLUS
DOCUMENT NUMBER: 94:145343
TITLE: Pharmaceutical composition containing a halomethyl-α-amino acid derivative for treatment of benign prostate hypertrophy
INVENTOR(S): Bey, P.; Jung, M.
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: Belg., 51 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 881210	A1	19800516	BE 1980-199013	19800117 <--
PRIORITY APPLN. INFO.:			US 1979-28739 A	19790410

AB The title compns. were prepared containing halomethyl-α-amino acid derivs. ZYC(NHR)COR1 [Y = FCH2, F2CH, F3C, ClCH2, Cl2CH; Z = R2NH(CH2)n, γ-guanidinopropyl; R,R2 = H, C1-4 alkyl, alkyl- or alkoxy carbonyl, etc.; n = 3,4; R1 = OH, C1-8 alkoxy, NR3R4; R3,R4 = H, C1-4 alkyl,

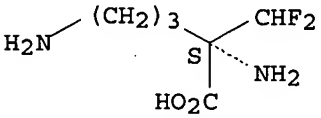
NHCHR5CO2H; R5 = H, C1-4 alkyl, PhCH2, etc.], e.g. α,δ-diamino-α-difluoromethylvaleric acid (I) [**70052-12-9**] or α-amino-α-fluoromethyl-δ-guanidinovaleric acid [73800-88-1], which had decarboxylase inhibiting properties in the formation of polyamines in the prostate. The compds. were prepd by treating ornithine or lysine ester derivs. having protected NH2 groups with a strong **base** to form the intermediate carbanion followed by reacting the product with the appropriate halomethyl halo alkylating agent and **hydrolyzing**. Lactams of these compds. were prepared by treating the amino acid esters with an appropiate **base**. A capsule formulation was prepared containing I 200, talc 5, and lactose 10 mg. The title compns. were also prepared as tablets and injections.

IT **70052-12-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing, for benign prostate hypertrophy treatment)
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



IT **69955-42-6P 70050-55-4P 70052-12-9P**
RL: PREP (Preparation)
(preparation of, for pharmaceuticals for treatment of benign prostate hypertrophy)
RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

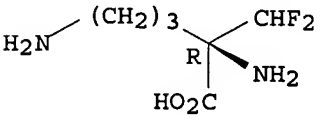
Absolute stereochemistry. Rotation (-).



● HCl

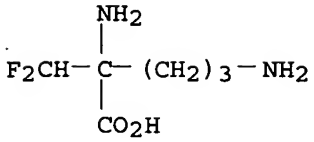
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

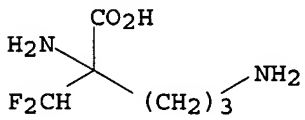
RN 70052-12-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:474865 CAPLUS
DOCUMENT NUMBER: 91:74865
TITLE: Direct synthesis of α-halogenomethyl-α-amino acids from the parent α-amino acids
AUTHOR(S): Bey, Philippe; Vevert, Jean Paul; Van Dorsselaer, Viviane; Kolb, Michael
CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, 67084, Fr.
SOURCE: Journal of Organic Chemistry (**1979**), 44(15), 2732-42
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 91:74865

AB α-Halomethyl amino acids H2NCRR1CO2H [I; R = Me, (CH2)3NH2, (CH2)4NH4, CH2CH2SMe, CH2Ph, CH2C6H4OH-p, CH2C6H3(OH)2-3,4, CH2CH2CO2H, imidazol-4-ylmethyl; R1 = CH2Cl, CH2F, CHF2, CBrF] were prepared by regioselective halomethylation of PhCH:NCHR2CO2Me [R2 = R except for (CH2)3N:CHPh, (CH2)4N:CHPh, CH2C6H4(OMe)2-3,4, CH2CH2CO2Me, 1-tritylimidazol-4-ylmethyl] by R1X (X = Cl, Br), cleaving the benzylidene from the resulting PhCH:NCR1R2CO2Me by acid, and by **hydrolyzing** the resulting H2NCR1R3CO2Me (R3 = R except for CH2C6H3(OMe)2-3,4, CH2CH2CO2Me). The mechanism of the alkylation step was discussed. I are potential inhibitors of the parent amino acid decarboxylases.

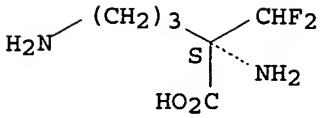
IT **68278-23-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and neutralization of)
RN 68278-23-9 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **69955-42-6P 70050-55-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 69955-42-6 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

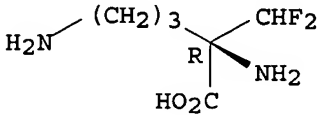
Absolute stereochemistry. Rotation (-).



● HCl

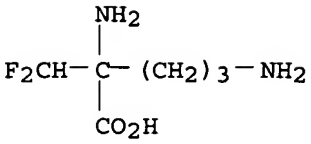
RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

L17 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:474273 CAPLUS
DOCUMENT NUMBER: 91:74273
TITLE: General approach to the synthesis of α-difluoromethyl amines as potential enzyme-activated irreversible inhibitors
AUTHOR(S): Bey, P.; Schirlin, D.
CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, Fr.
SOURCE: Tetrahedron Letters (**1978**), (52), 5225-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eight RCH(NH2)CHF2 [I, R = PhCH2, substituted benzyl, H2N(CH2)3] were prepared from RCH(CO2R1)CO2CMe3 (II, R = PhCH2, substituted benzyl, 3-phthalimidopropyl; R1 = Et, CMe3) in seven steps via the resp. RC(CHF2)(CO2H)CO2R1 (III) and by a Curtius rearrangement sequence. E.g., 3-MeOC6H4CH2CH(NH2)CHF2 was obtained from 3-MeOC6H4CH2CH(CO2Et)CO2CMe3. RC(NH2)(CHF2)CO2H [R = PhCH2, H2N(CH2)3] were obtained from the resp. III by Curtius rearrangement. The key step in the prepns. was the difluoromethylation of II by ClCHF2 and NaH. I [R = 3,4-(HO)2C6H3CH2], obtained from I [R = 3,4-(MeO)2C6H3CH2], and I [R = H2N(CH2)3] inhibited irreversibly L-aromatic-α-amino acid decarboxylase and ornithine decarboxylase, resp.
IT **71045-64-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 71045-64-2 CAPLUS
CN Ornithine, 2-(difluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L17 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:187335 CAPLUS
DOCUMENT NUMBER: 90:187335
TITLE: Halomethylated α-amino acids
INVENTOR(S): Bey, Philippe; Jung, Michel
PATENT ASSIGNEE(S): Merrell Toraude S. A., Fr.
SOURCE: Belg., 46 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 868882	A1	19781103	BE 1978-189191	19780710 <--
CA 1091661	A1	19801216	CA 1978-304918	19780607 <--
ZA 7803349	A	19790627	ZA 1978-3349	19780612 <--
IL 54912	A1	19841130	IL 1978-54912	19780615 <--
AU 7837327	A1	19800103	AU 1978-37327	19780621 <--
AU 522660	B2	19820617		
GB 2001960	A	19790214	GB 1978-27967	19780627 <--
GB 2001960	B2	19820224		
DE 2828739	A1	19790201	DE 1978-2828739	19780630 <--
DE 2828739	C2	19891207		
DK 7803094	A	19790112	DK 1978-3094	19780710 <--
DK 148322	B	19850610		
DK 148322	C	19851104		
SE 7807691	A	19790112	SE 1978-7691	19780710 <--
SE 444934	B	19860520		
SE 444934	C	19860828		
ES 471596	A1	19791001	ES 1978-471596	19780710 <--
FR 2430418	A1	19800201	FR 1978-20517	19780710 <--
FR 2430418	B1	19840713		
CH 642055	A	19840330	CH 1978-7466	19780710 <--
NL 7807453	A	19790115	NL 1978-7453	19780711 <--
NL 190662	B	19940117		
NL 190662	C	19940616		
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JP 01022259	B4	19890425		
ES 478610	A1	19790716	ES 1979-478610	19790314 <--
ES 478611	A1	19790716	ES 1979-478611	19790314 <--
ES 478612	A1	19790916	ES 1979-478612	19790314 <--
US 4496588	A	19850129	US 1983-487243	19830428 <--
US 4560795	A	19851224	US 1984-577116	19840206 <--
JP 63246365	A2	19881013	JP 1987-330367	19871228 <--
JP 03025424	B4	19910405		
US 5614557	A	19970325	US 1995-403531	19950314 <--

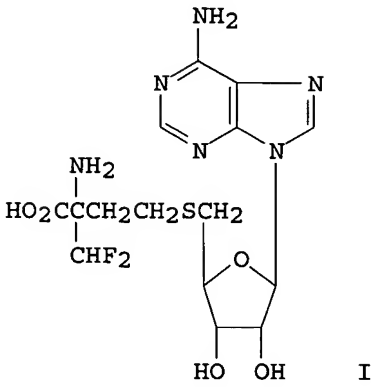
PRIORITY APPLN. INFO.:

US 1977-814765	A	19770711
US 1979-28757	B1	19790410
US 1979-28758	A1	19790410
US 1979-53937	A1	19790702

US 1980-204749	B2	19801107
US 1981-262834	B1	19810512
US 1982-382265	B3	19820526
US 1982-392051	A3	19820625
US 1982-373198	A1	19820929
US 1984-639977	B1	19840810
US 1987-110639	B1	19871015
US 1988-228789	B1	19880804
US 1989-334733	B1	19890406
US 1989-431685	B1	19891103
US 1990-534008	B1	19900601
US 1991-759633	B1	19910912
US 1992-874989	B1	19920424
US 1993-2521	B1	19930111
US 1993-137397	B1	19931014
US 1994-284706	B1	19940802

OTHER SOURCE(S): CASREACT 90:187335

GI



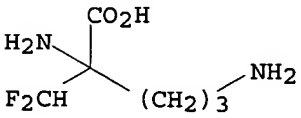
I

AB RNHCR1R2COR3 (R = H, acyl, alkoxycarbonyl: R1 = CH2F, CHF2, CF3, CH2Cl, CHCl2; R2 = CH2CH2SMe, CH2CH2SH, CH2CH2SCH2Ph, 5'-deoxy-5'-adenosylthioethyl, guanidinopropyl, (CH2)nNHR where n = 3 or 4, CH2CH2S2CH2CH2CR1(NH2)CO2H; R3 = OH, alkoxy, amino) and their lactams and salts were prepared Thus, NaSCH2CH2C(CHF2)(NH2)CO2Na was treated with 5'-O-tosyladenosine to give homocysteine-adenosine derivative I.

IT **68278-23-9P 69955-42-6P 70050-55-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 68278-23-9 CAPLUS

CN Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

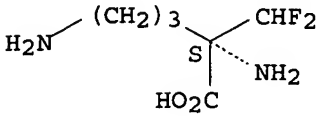


● HCl

RN 69955-42-6 CAPLUS

CN L-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

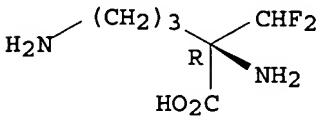
Absolute stereochemistry. Rotation (-).



● HCl

RN 70050-55-4 CAPLUS
CN D-Ornithine, 2-(difluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

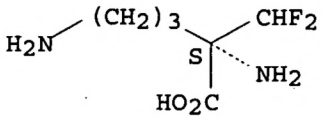
Absolute stereochemistry. Rotation (+).



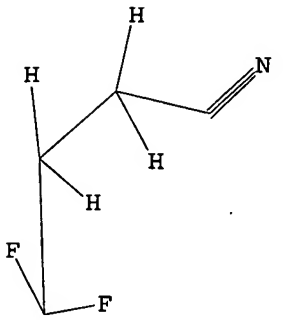
● HCl

L17 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:419036 CAPLUS
DOCUMENT NUMBER: 89:19036
TITLE: Catalytic irreversible inhibition of mammalian ornithine decarboxylase (E.C.4.1.1.17) by substrate and product analogs
AUTHOR(S): Metcalf, B. W.; Bey, P.; Danzin, C.; Jung, M. J.; Casara, P.; Vevert, J. P.
CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, Fr.
SOURCE: Journal of the American Chemical Society (**1978**), 100(8), 2551-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ornithine analogs incorporating an α-Me group functionalized by fluoro, chloro, and **cyano** substituents, as well as the putrescine analogs 5-hexyne-1,4-diamine (I) and trans-hex-2-ene-5-yne-1,4-diamine (II), were catalytic irreversible inhibitors of a preparation of mammaliam ornithine decarboxylase. For the ornithine analogs, it is proposed that decarboxylation of the enzyme-bound Schiff's base formed between pyridoxal phosphate and the analog leads to a reactive imine which can alkylate a nucleophilic residue at the enzyme's active site. Enzyme inactivation by I and II is rationalized on the basis of the microscopic reversibility principle. It is proposed that the proton abstraction implicit in the reverse reaction leads to a reactive allene in the active site, which, once again, is an alkylating agent.
IT **66640-93-5**
RL: BIOL (Biological study)
(ornithine decarboxylase inhibition by, kinetics and mechanism of)
RN 66640-93-5 CAPLUS
CN L-Ornithine, 2-(difluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).


H2N
(CH2)3
S
CHF2
NH2
HO2C

> d
L12 HAS NO ANSWERS
L12 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l12
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 18:36:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 61 TO ITERATE

100.0% PROCESSED 61 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 752 TO 1688
PROJECTED ANSWERS: 2 TO 123

L13 2 SEA SSS SAM L12

L14 3 L13

=> s l14 and reduc?
1908750 REDUC?
L15 0 L14 AND REDUC?

=> s l12 full
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 18:37:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1256 TO ITERATE

100.0% PROCESSED 1256 ITERATIONS 40 ANSWERS
SEARCH TIME: 00.00.01

L16 40 SEA SSS FUL L12

L17 51 L16

=> s l17 and reduc?
1908750 REDUC?
L18 4 L17 AND REDUC?

=> d 1-4 ibib abs hitstr

L18 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:596112 CAPLUS
DOCUMENT NUMBER: 125:221184
TITLE: Improved process for **reductive** hydrolysis of nitriles
INVENTOR(S): Beatty, Richard Paul
PATENT ASSIGNEE(S): E. I. Du Pont de Nemours & Co., USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9623753	A1	19960808	WO 1996-US749		19960122
W: CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5741955	A	19980421	US 1995-544227		19951017
EP 807098	A1	19971119	EP 1996-903570		19960122
EP 807098	B1	19980909			
R: CH, DE, ES, FR, GB, IT, LI, NL					
JP 10513447	T2	19981222	JP 1996-523580		19960122
PRIORITY APPLN. INFO.:			US 1995-381597	A	19950131
			US 1995-544227	A	19951017
			WO 1996-US749	W	19960122

OTHER SOURCE(S): CASREACT 125:221184; MARPAT 125:221184
AB This invention concerns processes for the **reductive** hydrolysis of nitriles to alcs. utilizing as a catalyst a transition metal complex of the formula MHZ(CO)Ln(PR3)2 wherein M is a transition metal selected from the group consisting of Fe, Ru and Os; Z is an anionic ligand; L is a neutral ligand; n is 0 or 1; and PR3 is a phosphine ligand. The title process gives high yields of alcs.
IT **26649-23-0 26649-25-2 26649-26-3**
140834-59-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved process for **reductive** hydrolysis of nitriles)
RN 26649-23-0 CAPLUS
CN Heptanenitrile, 4,4,5,5,6,6,7,7,7-nonafluoro- (8CI, 9CI) (CA INDEX NAME)

$F_3C-(CF_2)_3-CH_2-CH_2-CN$

RN 26649-25-2 CAPLUS
CN Nonanenitrile, 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro- (8CI, 9CI) (CA INDEX NAME)

$F_3C-(CF_2)_5-CH_2-CH_2-CN$

RN 26649-26-3 CAPLUS
CN Undecanenitrile, 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoro- (8CI, 9CI) (CA INDEX NAME)

$F_3C-(CF_2)_7-CH_2-CH_2-CN$

RN 140834-59-9 CAPLUS
CN Tridecanenitrile, 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,13,13,13-heneicosafluoro- (9CI) (CA INDEX NAME)

$F_3C-(CF_2)_9-CH_2-CH_2-CN$

L18 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:68387 CAPLUS
DOCUMENT NUMBER: 96:68387
TITLE: Compounds having a perfluoroalkyl group prepared in acid media containing zinc
INVENTOR(S): Blancou, Hubert Jean; Commeyras, Auguste Andre Aime; Teissedre, Robert
PATENT ASSIGNEE(S): Produits Chimiques Ugine Kuhlmann, Fr.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 38735	A1	19811028	EP 1981-400552	19810407
EP 38735	B1	19831130		
R: BE, CH, DE, FR, GB, NL, SE				
FR 2480742	A1	19811023	FR 1980-8721	19800418
FR 2480742	B1	19820319		
US 4478760	A	19841023	US 1981-249069	19810330
JP 56152427	A2	19811126	JP 1981-46576	19810331
JP 62041650	B4	19870903		
BR 8102329	A	19811208	BR 1981-2329	19810415
CA 1153775	A1	19830913	CA 1981-375637	19810416
PRIORITY APPLN. INFO.:			FR 1980-8721 A	19800418

AB RCHR1CHR2R3 (R = perfluoroalkyl; R1, R2 = H, alkyl, cycloalkyl, aryl, R3; R1R2 = alkylene; R3 = functional group, alkyl substituted functional group) were prepared by treating R1CH:CR2R3 with RI in the presence of Zn in a carboxylic acid solvent. Thus 446 g C6F13I was treated with 53 g CH2:CHCN in 400 g EtCO2H containing 68.3 g Zn and 2 g Cu(OAc)2 to give 70% C6F13CH2CH2CN.
IT **26649-25-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26649-25-2 CAPLUS
CN Nonanenitrile, 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro- (8CI, 9CI) (CA INDEX NAME)

$F_3C-(CF_2)_5-CH_2-CH_2-CN$

L18 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1973:420241 CAPLUS
DOCUMENT NUMBER: 79:20241
TITLE: Oil and stain-repellent compositions
PATENT ASSIGNEE(S): Allied Chemical Corp.
SOURCE: Brit., 9 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1296426	A	19721115	GB 1970-1296426	19700921
US 3646153	A	19720229	US 1969-867368	19691017
US 3657235	A	19720418	US 1969-867370	19691017
US 3697562	A	19721010	US 1969-867373	19691017
US 3754026	A	19730821	US 1969-867371	19691017
US 3786093	A	19740115	US 1969-867372	19691017
FR 2065912	A5	19710806	FR 1970-33539	19700916
JP 50002653	B4	19750128	JP 1970-89750	19701014
US 3767625	A	19731023	US 1971-205424	19711206
US 3852313	A	19741203	US 1973-362616	19730521
US 3899563	A	19750812	US 1973-381453	19730723
US 3839312	A	19741001	US 1973-382622	19730725

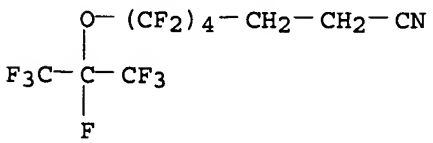
PRIORITY APPLN. INFO.:

US 1969-867368	A	19691017
US 1969-867370	A	19691017
US 1969-867371	A	19691017
US 1969-867372	A	19691017
US 1969-867373	A	19691017
US 1971-205424	A3	19711206

AB Nylon fibers containing 1-2% of an amide or isocyanate with C3F7O(CF2)m(CH2)n (m = 3 or 4; n = 0, 2, or 10) groups were oil- and stain-repellent. The F compds. **reduced** the surface energy of the fibers but did not affect their mech. props. comminuted nylon 6 pellets were treated with 1,7-bis[(4-perfluoroisopropoxy)butyryl]-1,4,7-triazaheptane monoglutaramide (I) [31794-63-5], dried at 70.deg. and 5 mm extruded and pelletized. The pellets were extruded at 260.deg. and 18-23 m/min into a filament containing 1% I. The surface energies of 60, 16, and 8 denier filaments were 18, 25, and 32 dynes/cm, resp. Annealing at 120-50.deg. for 2-4 hr lowered the surface energies of the 16 and 8 denier filaments to 18-22 and 25-7 dynes/cm, resp. The filaments were as receptive to dyes and as colorfast when laundered or dry-cleaned as unmodified filaments and dyeing had no adverse effect on the surface energies.

IT **28793-33-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with trioxane)

RN 28793-33-1 CAPLUS
CN Heptanenitrile, 4,4,5,5,6,6,7,7-octafluoro-7-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]- (9CI) (CA INDEX NAME)



L18 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1971:99476 CAPLUS
DOCUMENT NUMBER: 74:99476
TITLE: Telomers for use as surfactants

INVENTOR(S): Anello, Louis G.; Sweeney, Richard F.; Litt, Morton H.
PATENT ASSIGNEE(S): Allied Chemical Corp.
SOURCE: Fr., 43 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1599703	A	19700720	FR 1968-1599703	19680425
US 3514487	A	19700526	US 1967-633359	19670425
US 3758543	A	19730911	US 1967-633368	19670425
US 3697564	A	19721010	US 1968-721115	19680412
US 3706773	A	19721219	US 1968-721117	19680412
BE 714160	A	19680916	BE 1968-714160	19680424
NL 6805864	A	19681028	NL 1968-5864	19680425
GB 1224771	A	19710310	GB 1968-1224771	19680425
DE 1768286	A	19711028	DE 1967-1768286	19680425
BR 6898615	A0	19730104	BR 1968-198615	19680425
BR 6898619	A0	19730410	BR 1968-198619	19680425
US 3754009	A	19730821	US 1970-40341	19700525

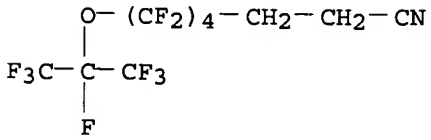
PRIORITY APPLN. INFO.:

US 1967-633359	A	19670425
US 1967-633368	A	19670425
US 1968-621115	A	19680412
US 1968-621117	A	19680412
US 1967-63368	A	19670425
US 1968-721115	A	19680412
US 1968-721117	A	19680412

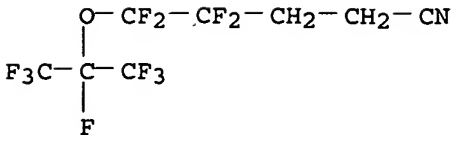
AB The preferred telomers having the general formula R(A)m(D)n(G)vY (I), where R = (CF3)2CFO(CF2)2; A = (CF2)2; D = (CH2)2; G = CH2 or CF2; m = n + 0-20, v = 0 or 1; m + n = 10; and Y = CN, CO2H, CO2Na, COCl, CO2Me, CONH2, or CONH(CH2)2OH, are prepared by known reactions starting with telomers of the formulas R(A)m(D)nE or R(A)m(D)n+1 E, where E = Br or iodo. Thus, 53 g (CF3)2CFO(CF2)2(CH2)2I reacted with 15 g NaCN in 50 ml Me2SO at 60° to give 29 g (CF3)2CFO(CF2)2(CH2)2CN, b10 68-9°. De-tails for preparation of >50 examples of I are given. The addition of 0.5% I (where m = v = 0, n = 5, and Y = CO2Na) **reduces** the surface tension of H2O to 18.4 dynes/cm. The amides are especially oil repellent and are useful in the treatment of textiles.

IT **28793-33-1P 28793-35-3P 32347-50-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

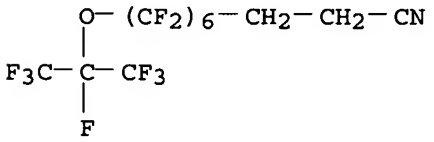
RN 28793-33-1 CAPLUS
CN Heptanenitrile, 4,4,5,5,6,6,7,7-octafluoro-7-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 28793-35-3 CAPLUS
CN Pentanenitrile, 4,4,5,5-tetrafluoro-5-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 32347-50-5 CAPLUS
CN Nonanenitrile, 4,4,5,5,6,6,7,7,8,8,9,9-dodecafluoro-9-[tetrafluoro-1-(trifluoromethyl)ethoxy]- (8CI) (CA INDEX NAME)



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